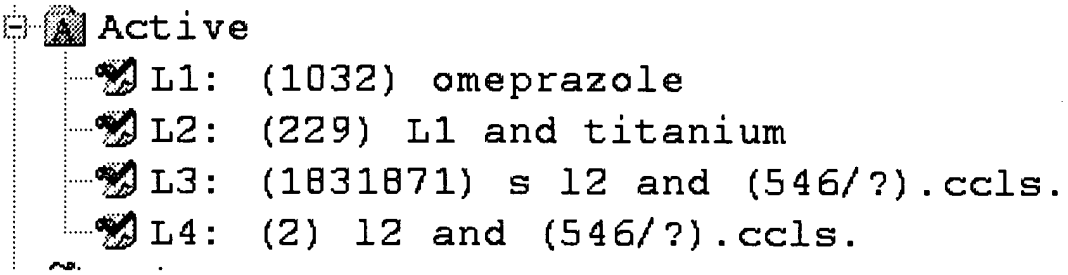
EAST 10/608,781

BLS

- Active
  - L1: (1032) omeprazole
  - L2: (354) l1 and complex
  - L3: (6) l2 and chelate
  - L4: (2) l2 and (546/?)".ccls"


Active
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L2: (229) L1 and titanium
L3: (1831871) s l2 and (546/?).ccls.
L4: (2) l2 and (546/?).ccls.

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=> s omeprazole
L1          3823 OMEPRAZOLE

=> s l1 and chelate
          42702 CHELATE
L2            3 L1 AND CHELATE

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                   data from INPADOC
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                   fields
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 NEWS  15 APR 25   Patent searching, including current-awareness alerts (SDIs),
                   based on application date in CA/CAplus and USPATFULL/USPAT2
                   may be affected by a change in filing date for U.S.
                   applications.
 NEWS  16 APR 28   Improved searching of U.S. Patent Classifications for
                   U.S. patent records in CA/CAplus
 NEWS  17 MAY 23   GBFULL enhanced with patent drawing images
 NEWS  18 MAY 23   REGISTRY has been enhanced with source information from
                   CHEMCATS
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                   (Version 8.0 for Windows) now available
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 NEWS  22 JUN 13   FRFULL enhanced with patent drawing images
 NEWS  23 JUN 20   MEDICONF to be removed from STN
 NEWS  24 JUN 27   MARPAT displays enhanced with expanded G-group definitions
                   and text labels

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               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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=> dis his

     (FILE 'HOME' ENTERED AT 10:18:50 ON 28 JUN 2005)

     FILE 'CAPLUS' ENTERED AT 10:19:10 ON 28 JUN 2005

=> s omeparzole
L1             1 OMEPARZOLE

=> s omeprazole
L2          3823 OMEPRAZOLE

=> s l2 and complex
       1204140 COMPLEX
L3            83 L2 AND COMPLEX

=> s l2 and chelate
```

42702 CHELATE
L4 3 L2 AND CHELATE

=> d 1-3 fbib abs fhitstr

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:1041824 CAPLUS
DN 142:80101
TI Spectrophotometric determination of **omeprazole** and pantoprazole sodium via chelates with iron, chromium, and cobalt
AU Salama, F.; El-Abasawy, N.; Razeq, S. A. Abdel; Ismail, M. F.; Fouad, M. M.
CS Pharmaceutical chemistry Department, Faculty of Pharmacy (Boys), Al-Azhar University, Cairo, Egypt
SO Bulletin of the Faculty of Pharmacy (Cairo University) (2003), 41(1), 185-196
CODEN: BFPHA8; ISSN: 1110-0931
PB Cairo University, Faculty of Pharmacy
DT Journal
LA English
AB Spectrophotometric procedures for the determination of 2 irreversible proton pump inhibitors, **omeprazole** and pantoprazole sodium were developed, the procedures are based on the formation of 2 : 1 chelates of both drugs with different metal ions. Pantoprazole sodium is quantified by a stability-indicating procedure through chelation with iron (III) in aqueous-ethanol medium to form an orange **chelate** picked at 455 nm. The procedure retains its accuracy in presence of ≤ 70% of its degradate, sulfenic acid prepared by degrading the pure drug in borate buffer of pH 8 at 37°C for 5 days. The colored chelates of **omeprazole** in ethanol are determined spectrophotometrically at 411 nm, 339 nm and 523 nm using iron (III), chromium (III), and cobalt (II), resp. Regression anal. of Beer's plots showed good correlation in the concentration range of 15-95 μg ml-1, 10-60 μg ml-1, and 15-150 μg ml-1 of pure **omeprazole** using iron (III), chromium (III), and cobalt (II), resp. and in the range of 30-300 μg ml-1 of pantoprazole sodium using iron (III). The limits of detection are 0.22 - 3.65 μg ml-1. The optimum assay conditions are investigated and the recovery of the cited drugs from their dosage forms ranges from 97.2 to 100.3%. Good values of precision are obtained, intraday RSD are 0.93-1.75% and the interday RSD are 0.51-3.29%.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:783863 CAPLUS
DN 140:65345
TI Validation of the spectrophotometric determination of **omeprazole** and pantoprazole sodium via their metal chelates
AU Salama, F.; El-Abasawy, N.; Abdel Razeq, S. A.; Ismail, M. M. F.; Fouad, M. M.
CS Faculty of Pharmacy, Pharmaceutical Chemistry Department, Al-Azhar University, Cairo, Nasr City, 11454, Egypt
SO Journal of Pharmaceutical and Biomedical Analysis (2003), 33(3), 411-421
CODEN: JPBADA; ISSN: 0731-7085
PB Elsevier Science B.V.
DT Journal
LA English
AB Spectrophotometric procedures for the determination of 2 irreversible proton pump inhibitors, **omeprazole** (OMZ) and pantoprazole (PNZ) sodium were developed, the procedures are based on the formation of 2:1 chelates of both drugs with different metal ions. Pantoprazole sodium is quantified by a stability-indicating procedure through chelation with iron (III) in

aqueous-ethanol medium to form an orange **chelate** picked at 455 nm. The procedure retains its accuracy in presence of ≤ 70% of its degradate, sulfenic acid prepared by degrading the pure drug in borate buffer of pH 8 at 37 °C for 5 days. The colored chelates of OMZ in EtOH are determined spectrophotometrically at 411, 339, and 523 nm using iron (III), chromium (III), and cobalt (II), resp. Regression anal. of Beer's plots showed good correlation in the concentration range of 15-95, 10-60, and 15-150 μg ml-1 of pure OMZ using iron (III), chromium (III), and cobalt (II), resp., and in the range of 30-300 μg ml-1 of PNZ sodium using iron (III). The limits of detection are 0.22-3.65 μg ml-1 while limits of quantitation range between 0.74 and 12.17 μg ml-1. The optimum assay conditions are investigated and the recovery of the cited drugs from their dosage forms ranges from 97.2 to 100.3%. Good values of precision are obtained, intraday R.S.D. are 0.93-1.75% and the inter day R.S.D. are 0.51-3.29%.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:554614 CAPLUS
DN 125:256568
TI A study of the stripping voltammetric behavior of selected metal chelates and its application to automated analysis of river waters
AU Maxwell, Tracy J.; Smyth, W.Franklin
CS ABCS School, Univ. Ulster, Coleraine, BT52 1SA, UK
SO Electroanalysis (1996), 8(8-9), 795-802
CODEN: ELANEU; ISSN: 1040-0397
PB VCH
DT Journal
LA English
AB The anodic and adsorptive stripping voltammetry (ASV and AdSV) behavior of Zn2+, Cd2+, Pb2+, Cu2+, Ni2+, and Sn4+ in the presence of selected complexing/chelated agents was studied. The presence of 2,5-dimercapto-1,3,4-thiadiazole lowers the limit of detection (LOD) for the ASV determination of Zn2+, Cd2+, and Pb2+ in 5 + 10-3 mol dm-3 LiCl supporting electrolyte with a deposition time of 120 s to 0.82, 0.17, and 0.34 ppb, resp., due to participation of the adsorbed complexing agent in the overall process. Similarly, Cd2+ was determined in the presence of benzimidazole sulfoxides (I) and (II) by ASV in Britton-Robinson (BR) buffer pH 9 with 120 s deposition with lower LODs of 0.12 and 0.06 ppb, resp. AdSV was also used to determine Cd2+ with I, II, and ammonium pyrrolidine dithiocarbamate (III) with LODs of 0.70, 0.64, and 0.20 ppb, resp., and with Zn2+ having an AdSV LOD of 1.09 ppb using adsorption of its **chelate** with III at -900 mV for 60 s in a supporting electrolyte of 5 + 10-3 mol dm-3 LiCl. Participation of the adsorbed complexing agent in the ASV process is also observed for Sn4+ and Cu2+ in an oxalate/NH4Cl/HCl buffer with lowered LODs of 0.51 ppb and 0.76 ppb in the presence of p-methylene blue. The chelating agent 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol was used to determine Cd2+, Zn2+, and Pb2+ using the AdSV technique down to LODs of 9.3, 2.7, and 6.3 ppb, resp. The methods were combined in the development of an automated method for the determination of Zn, Cd, Pb, and Cu traces in an artificial river water matrix. Determination of Ni, Sn, and As by the automated method and in such a matrix proved to be inaccurate.

=> dis his

(FILE 'HOME' ENTERED AT 10:18:50 ON 28 JUN 2005)

FILE 'CAPLUS' ENTERED AT 10:19:10 ON 28 JUN 2005
L1 1 S OMEPARZOLE
L2 3823 S OMEPRAZOLE
L3 83 S L2 AND COMPLEX

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L4            3 S L2 AND CHELATE

=> s l2 and purification
        308941 PURIFICATION
L5           8 L2 AND PURIFICATION

=> d 1-8 fbib abs fhitstr

L5   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2002:594991  CAPLUS
DN   137:136920
TI   Purification and pharmaceutical and food industry use of
     carbonic anhydrase VI from milk
IN   Karhumaa, Pepe; Kaunisto, Kari; Leinonen, Jukka; Parkkila, Seppo;
     Rajaniemi, Hannu
PA   Oulun Yliopisto, Finland
SO   PCT Int. Appl., 49 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2002061066         A1    20020808    WO 2002-FI81            20020201
     WO 2002061066         C1    20031106
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                          FI 2001-193          A  20010201
                                          FI 2001-845          A  20010424
     FI 2001000845         A     20020802  FI 2001-845             20010424
                                          FI 2001-193          A  20010201
AB   This invention relates to a new method for preparing an enzyme preparation
     comprising carbonic anhydrase VI (CA VI). The method comprises that CA VI
     is isolated from human milk or from the milk of a milk-producing animal,
     such as cow, goat or sheep. CA VI may be purified until homogeneity or
     until a chosen purity level depending on the use of the enzyme preparation The
     enzyme preparation may be used for preparing pharmaceutical compns., in
     particular, a composition for the prevention of caries, or for preparing food
     compns., in particular, an infant milk formula composition
RE.CNT  6     THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5   ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2000:53615  CAPLUS
DN   132:78557
TI   Oxidative process of synthesis of 5-methoxy-2-[(4-methoxy-3,5-dimethyl-2-
     pyridyl)methyl]sulfinyl-1H-benzimidazole with precipitative
     purification
IN   Hafner Milac, Natasa; Jereb, Darja
PA   Lek, Tovarna Farmacevtskih in Kemicnih Izdelkov, D.D., Slovenia
SO   PCT Int. Appl., 12 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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PI	WO 2000002876	A1	20000120	WO 1999-SI20	19990712
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				SI 1998-196	A 19980713
	SI 20019	C	20000229	SI 1998-196	19980713
	AU 9946714	A1	20000201	AU 1999-46714	19990712
				SI 1998-196	A 19980713
				WO 1999-SI20	W 19990712
	EP 1095037	A1	20010502	EP 1999-930107	19990712
	EP 1095037	B1	20020417		
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				SI 1998-196	A 19980713
				WO 1999-SI20	W 19990712
	NZ 509000	A	20011221	NZ 1999-509000	19990712
				SI 1998-196	A 19980713
				WO 1999-SI20	W 19990712
	AT 216382	E	20020515	AT 1999-930107	19990712
				SI 1998-196	A 19980713
				WO 1999-SI20	W 19990712
	RU 2197486	C2	20030127	RU 2001-103900	19990712
				SI 1998-196	A 19980713
				WO 1999-SI20	W 19990712
	CZ 293653	B6	20040616	CZ 2001-123	19990712
				SI 1998-196	A 19980713
	US 6268502	B1	20010731	US 2000-463651	20000830
				SI 1998-196	A 19980713
				WO 1999-SI20	W 19990712
	US 2002007069	A1	20020117	US 2001-919068	20010730
				SI 1998-196	A 19980713
				WO 1999-SI20	W 19990712
				US 2000-463651	A1 20000830

OS CASREACT 132:78557

AB 5-Methoxy-2-[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl-1H-benzimidazole (**omeprazole**) is readily prepared by the liquid-phase oxidation of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]thio]benzimidazole with 3-chloroperoxybenzoic acid in Et acetate, where **omeprazole** is poorly soluble, at -10° to +5°. The crude **omeprazole** is then purified by dissoln. into an aqueous methylamine solution, followed by precipitation under the addition of hydrochloric acid.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:732170 CAPLUS

DN 131:314263

TI **Purification** of **omeprazole**

IN Ge, Jilong; Yan, Yimin; Tu, Yongrui

PA Changzhou No.4 Pharmaceutical Plant, Peop. Rep. China

SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV

DT Patent

LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1160050	A	19970924	CN 1996-116288	19960320
	CN 1053444	B	20000614		
				CN 1996-116288	19960320

AB **Omeprazole** is refined by dissolving crude **omeprazole** in water, treating with NaOH or KOH for 0.5-2 h by controlling the pH at 10.5-11.5, decoloring with activated C, adding organic solvent, stirring at 0-35°, adding solid acid in batch, crystallizing with the pH controlled at 7.0-8.5, filtering, washing with water, and drying at 40°. **Omeprazole** may be refined by dissolving crude **omeprazole** in organic solvent, treating with NaOH or KOH, decoloring, adding water, and operating by the above method. The organic solvent is selected from C1-8 alkyl alc., acetone, THF, dioxane, acetonitrile, and other solvent dissolved in water. The mole ratio of **omeprazole** to NaOH is 1:1.

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:262326 CAPLUS
DN 126:238299
TI Preparation and **purification** of Form I and Form II of ranitidine hydrochloride
IN Yoo, Seo Hong
PA USA
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9707112	A1	19970227	WO 1996-US13246	19960816
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
				US 1995-515790	A 19950816
	US 5686588	A	19971111	US 1995-515790	19950816
	CA 2227264	AA	19970227	CA 1996-2227264	19960816
	CA 2227264	C	20021022		
				US 1995-515790	A 19950816
	AU 9667255	A1	19970312	AU 1996-67255	19960816
	AU 713507	B2	19991202		
				US 1995-515790	A 19950816
				WO 1996-US13246	W 19960816
	EP 859768	A1	19980826	EP 1996-927432	19960816
	EP 859768	B1	20030108		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
				US 1995-515790	A 19950816
				WO 1996-US13246	W 19960816
	CN 1198744	A	19981111	CN 1996-197336	19960816
				US 1995-515790	A 19950816
	BR 9610288	A	19990727	BR 1996-10288	19960816
				US 1995-515790	A 19950816
				WO 1996-US13246	W 19960816
	JP 11508601	T2	19990727	JP 1996-509483	19960816
				US 1995-515790	A 19950816
				WO 1996-US13246	W 19960816
	AT 230737	E	20030115	AT 1996-927432	19960816
				US 1995-515790	A 19950816

WO 1996-US13246 W 19960816

AB A stoichiometric acid moiety transfer reaction for the preparation of an acid salt of an amine compound such as ranitidine is described. The acid moiety transfer reaction provides amine acid salts of high purity and having crystalline structure of uniform size and shape. Thus, treatment of ranitidine free base in a mixture of industrial methylated spirits and EtOAc with 2,5-dimethylpyridine.HCl afforded Form I ranitidine hydrochloride which was free from contamination from Form II.

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:204119 CAPLUS
DN 126:186087
TI Optical **purification** of enantiomerically enriched 2-[(arylmethyl)sulfinyl]benzimidazole derivatives
IN Von Unge, Sverker
PA Astra Aktiebolag, Swed.; Von Unge, Sverker
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9702261	A1	19970123	WO 1996-SE841	19960626
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
			US 1995-491939	A2 19950703
			WO 1995-SE817	A 19950703
ZA 9605205	A	19970103	ZA 1996-5205	19960619
			WO 1995-SE817	A 19950703
TW 444010	B	20010701	TW 1996-85107517	19960622
			WO 1995-SE817	A 19950703
CA 2226184	AA	19970123	CA 1996-2226184	19960626
			WO 1995-SE817	A 19950703
AU 9663240	A1	19970205	AU 1996-63240	19960626
AU 698638	B2	19981105		
			WO 1995-SE817	A 19950703
			WO 1996-SE841	W 19960626
EP 836601	A1	19980422	EP 1996-922339	19960626
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			WO 1995-SE817	W 19950703
			WO 1996-SE841	W 19960626
CN 1193971	A	19980923	CN 1996-196465	19960626
CN 1098261	B	20030108		
			WO 1995-SE817	A 19950703
BR 9609450	A	19990302	BR 1996-9450	19960626
			WO 1995-SE817	W 19950703
			WO 1996-SE841	W 19960626
JP 11508590	T2	19990727	JP 1996-505063	19960626
			WO 1995-SE817	A 19950703
			WO 1996-SE841	W 19960626
RU 2144031	C1	20000110	RU 1998-101727	19960626
			WO 1995-SE817	A 19950703
			WO 1996-SE841	W 19960626
IL 122811	A1	20001121	IL 1996-122811	19960626
			WO 1995-SE817	A 19950703
			WO 1996-SE841	W 19960626
EE 3444	B1	20010615	EE 1997-368	19960626
			WO 1995-SE817	A 19950703

				WO 1996-SE841	W	19960626
PL 186702		B1	20040227	PL 1996-324394		19960626
				WO 1995-SE817	A	19950703
				WO 1996-SE841	W	19960626
EP 1498416		A1	20050119	EP 2004-24339		19960626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI						
				WO 1995-SE817	A	19950703
				EP 1996-922339	A3	19960626
US 5929244		A	19990727	US 1996-676215		19960719
				WO 1995-SE817	A	19950703
				WO 1996-SE841	W	19960626
NO 9706030		A	19980209	NO 1997-6030		19971222
NO 313008		B1	20020729			
				US 1995-491939	A	19950703
				WO 1995-SE817	A	19950703
				WO 1996-SE841	W	19960626

AB The title process for purification of, e.g., **omeprazole** comprises crystallization of the racemate from a solution of an enantiomerically or diastereomerically enriched preparation followed by recovery of the purified. compound

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:645838 CAPLUS
DN 121:245838
TI Co-**purification** of gastric mucoproteins with DNA:. An explanation for the reported 'interaction' of **omeprazole** with DNA in rat tissues
AU Adams, Stephen P.; Laws, George M.; Storer, Richard D.; Kraynak, Andrew R.; DeLuca, John G.; Nichols, Warren W.
CS Genetic and Cellular Toxicology, Merck Research Laboratories, West Point, PA 19486, USA
SO Mutation Research (1994), 322(4), 307-20
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier
DT Journal
LA English
AB Recently, Phillips et al. reported that small amts. of radioactivity derived from [14C]**omeprazole** were 'associated' with DNA purified from gastrointestinal tissues of treated rats (Mutagenesis 7, 277-283, 1992). The authors hypothesized that this radioactivity arose from **omeprazole** bound to contaminating protein in the DNA fraction (Mutagenesis 7, 395-396, 1992). Using rats injected with 35S-labeled amino acids, the authors found significant protein contamination (0.06 μg of protein per μg of DNA) in DNA purified from gastrointestinal tissues. Gastric mucous proteins represent likely candidates for binding of **omeprazole** in the rat model used by Phillips et al. To investigate this, the authors partially purified proteins from gastric mucus, incubated them with [14C]**omeprazole**, and then added these radiolabeled mucoproteins to homogenates of rat colon and duodenum before starting the DNA purification Detectable amts. of the added mucoproteins remained in the DNA fraction, but none of the control protein, bovine serum albumin, remained with the DNA. Further characterization of the mucoproteins by hydroxyapatite chromatog. indicated that a certain population of these proteins survived the DNA purification procedures. These data indicate that the association of **omeprazole** with DNA reported by Phillips et al. most probably is explained by binding of **omeprazole** to mucous glycoproteins (or other proteins present in the GI tract) that selectively survive DNA purification protocols.

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1990:134975 CAPLUS
DN 112:134975
TI **Purification** and characterization of hydrogen ion-potassium

ATPase from hog gastric mucosa
AU Hongo, Toshio; Nojima, Shoshichi; Setaka, Morio
CS Fac. Pharm. Sci., Teikyo Univ., Sagamiko, 199-01, Japan
SO Japanese Journal of Pharmacology (1990), 52(2), 295-305
CODEN: JJPAAZ; ISSN: 0021-5198
DT Journal
LA English
AB A (H+ + K+)-ATPase-enriched membrane fraction derived from the fundic portion of hog gastric mucosa was obtained by a combination of differential and repeated 7% Ficoll gradient centrifugation. The microsomal membrane fraction isolated by repeated 7% Ficoll gradient centrifugation was free of ouabain-sensitive (Na+ + K+)-ATPase, 5'-nucleotidase, and succinate dehydrogenase; and it was highly enriched in (H+ + K+)-ATPase and K+-stimulated p-nitrophenylphosphatase (p-NPPase). The (H+ + K+)-ATPase had a pH optimum of 7.4 and was stimulated by Tl+, K+, Rb+, and NH4+ with Ka values of 0.0667, 0.526, 0.667, and 3.03 mM, resp., at this pH. On the other hand, monovalent cations such as Na+, Li+ and (CH3)4N+ as well as divalent cations such as Cu2+, Ca2+, Ba2+, Sr2+, and Cd2+ inhibited this enzyme activity in a concentration-dependent manner. Ouabain and oligomycin had no effect, whereas **omeprazole**, a specific (H+ + K+)-ATPase inhibitor, inhibited this enzyme activity in a pH-dependent manner. SDS-PAGE showed a major band (≥90% of protein) at 97,400 daltons, which was phosphorylated in the presence of Mg2+ and [γ-32P]ATP and dephosphorylated in the presence of K+. The present method was very simple, and the (H+ + K+)-ATPase activity of the microsomal fraction obtained by this method was much higher compared with those obtained by other methods such as free-flow electrophoresis.

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:434336 CAPLUS
DN 109:34336
TI **Purification** and properties of a vanadate- and N-ethylmaleimide-sensitive ATPase from chromaffin granule membranes
AU Moriyama, Yoshinori; Nelson, Nathan
CS Roche Inst. Mol. Biol., Roche Res. Cent., Nutley, NJ, 07110, USA
SO Journal of Biological Chemistry (1988), 263(17), 8521-7
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB A vanadate- and N-ethylmaleimide-sensitive ATPase was purified .apprx.500-fold from chromaffin granule membranes. The purified preparation contained a single major polypeptide with an apparent mol. mass of .apprx.115 kDa, which was copurified with the ATPase activity. Immunol. studies revealed that this polypeptide has no relation to subunit I [115 kilodaltons (kDa)] of the H+-ATPase from chromaffin granules. The ATPase activity of the enzyme is inhibited .apprx.50% by 100 μM N-ethymaleimide or 5 μM vanadate. The enzyme is not sensitive to DCCD, ouabain, SCH28080, or **omeprazole**, which distinguishes it from Na+/K+-ATPase and the gastric K+/H+-ATPase. ATP and 2-dATP are equally effective substrates for the enzyme. However, the enzyme exhibited only 10% activity with GTP as a substrate. UV illumination of the purified enzyme in the presence of [α-32P]ATP exclusively labeled the 115-kDa protein. This labeling was increased by Mg2+ and strongly inhibited by Ca2+ ions. Similarly, the ATPase activity was dependent on Mg2+ and inhibited by the presence of Ca2+ ions. The ATPase activity of the enzyme was largely insensitive to monovalent anions and cations, except for F-, which inhibited the vanadate-sensitive ATPase. Incubation of the enzyme in the presence of [14C]N-ethylmaleimide labeled the 115-kDa polypeptide, and this labeling could be prevented by the addition of ATP dueing the incubation. A reciprocal experiment showed that preincubation with N-ethylmaleimide inhibited the labeling of the 115-kDa polypeptide by [α-32P]ATP by UV illumination. This suggests a close proximity between the ATP-binding site and an essential SH group. A possible connection between the isolated ATPase and organelle movement is

discussed.

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     FILE 'CAPLUS' ENTERED AT 10:19:10 ON 28 JUN 2005
L1             1 S OMEPARZOLE
L2          3823 S OMEPRAZOLE
L3            83 S L2 AND COMPLEX
L4             3 S L2 AND CHELATE
L5             8 S L2 AND PURIFICATION

=> s l3 and purification
        308941 PURIFICATION
L6             0 L3 AND PURIFICATION

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 NEWS  8  MAR 22  KOREAPAT now updated monthly; patent information enhanced
 NEWS  9  MAR 22  Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  10 MAR 22  PATDPASPC - New patent database available
 NEWS  11 MAR 22  REGISTRY/ZREGISTRY enhanced with experimental property tags
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NEWS  12 APR 04  EPFULL enhanced with additional patent information and new
                 fields
NEWS  13 APR 04  EMBASE - Database reloaded and enhanced
NEWS  14 APR 18  New CAS Information Use Policies available online
NEWS  15 APR 25  Patent searching, including current-awareness alerts (SDIs),
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                 may be affected by a change in filing date for U.S.
                 applications.
NEWS  16 APR 28  Improved searching of U.S. Patent Classifications for
                 U.S. patent records in CA/CAplus
NEWS  17 MAY 23  GBFULL enhanced with patent drawing images
NEWS  18 MAY 23  REGISTRY has been enhanced with source information from
                 CHEMCATS
NEWS  19 JUN 06  STN Patent Forums to be held in June 2005
NEWS  20 JUN 06  The Analysis Edition of STN Express with Discover!
                 (Version 8.0 for Windows) now available
NEWS  21 JUN 13  RUSSIAPAT: New full-text patent database on STN
NEWS  22 JUN 13  FRFULL enhanced with patent drawing images
NEWS  23 JUN 20  MEDICONF to be removed from STN
NEWS  24 JUN 27  MARPAT displays enhanced with expanded G-group definitions
                 and text labels

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              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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=> s omeprazole(w)complex
3827 OMEPRAZOLE
1204477 COMPLEX
L1 6 OMEPRAZOLE(W)COMPLEX

=> d 1-6 fbib abs fhitstr

L1 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:855339 CAPLUS
DN 142:100340
TI Complex preparation for oral use
IN Min, Dong Seon
PA SK Chemicals Co., Ltd., S. Korea
SO Repub. Korea, No pp. given
CODEN: KRXXFC
DT Patent
LA Korean
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	KR 212960	B1	19990802	KR 1995-69028	19951230
				KR 1995-69028	19951230

AB A composite formulation for oral administering is provided for inhibiting secretion of gastric acid and for removing helicobacter pylori to reduce problems such as stomach ulcer. The composite formulation for oral administering to patient comprises an omeprazole and any antibiotics to inhibit helicobacter pylori in stomach. The omeprazole is encapsulated into a cyclodextrin compound and is coated by a coating agent dissolved within intestines. The omeprazole component contained in the composite formulation is able to release out from an entry of small intestines. After the release of omeprazole, the antibiotics is discharged to maximize the antibiotic activity and the effect to inhibit the helicobacter pylori.

L1 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:445783 CAPLUS
DN 138:68864
TI Homology modelling of human CYP2 family enzymes based on the CYP2C5 crystal structure
AU Lewis, D. F. V.
CS Molecular Toxicology Group, School of Biomedical and Life Sciences, University of Surrey, Guildford, GU2 7XH, UK
SO Xenobiotica (2002), 32(4), 305-323
CODEN: XENOBH; ISSN: 0049-8254
PB Taylor & Francis Ltd.
DT Journal
LA English
AB The construction of mol. models for human cytochromes P 450 from the CYP2 family are reported, utilizing the recently available crystal structure of CYP2C5, which is also a mammalian (rabbit) form of the enzyme. In particular, selective substrate interactions with CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 and CYP2E1 are described in the context of favorable contacts with active site amino acid residues that appear to orientate each substrate for metabolism at the exptl. observed position. The results are consistent with reported findings from site-directed

mutagenesis expts. with the CYP2 family, and with published information on substrate metabolism
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:344772 CAPLUS
DN 129:85945
TI Complexation of omeprazole with meglumine and its stability
AU Rhee, Gye Ju; Kim, Sung Wook; Do, Ki Chan; Park, Chong Bum; Hwang, Sun Joo
CS College of Pharmacy, Chungnam National Univ., S. Korea
SO Yakche Hakhoechi (1997), 27(4), 253-263
CODEN: YAHAEX; ISSN: 0259-2347
PB Korean Society of Pharmaceutics
DT Journal
LA Korean
AB To investigate the interaction of omeprazole (OMP) and meglumine (MEG), a complex was prepared by a freeze-drying method in ammoniacal aqueous medium at room temperature and subjected to IR, DSC, and NMR anal. In addition, the stability of the complex was tested by accelerated stability anal., and the dissoln. rate of both powder and enteric coated pellets was determined the by paddle method. IR, DSC, and 1H NMR studies indicate the formation of inclusion complex between OMP and MEG in a stoichiometric ratio (1:1) of OMP:MEG. The dissoln. rate of the enteric coated OMP-MEG complex pellet in simulated enteric fluid was 90.6% in 10 min, which may satisfy the requirements for the regulation of dissoln. The OMP-MEG complex decomposed according to the pseudo 1st-order kinetics. OMP was stabilized markedly by the formation of the OMP-MEG complex, and the humidity increased the stability of OMP-MEG complex by decreasing the decomposition rate.

L1 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:85140 CAPLUS
DN 124:211738
TI A comparative study on the pharmaceutical properties of rectal suppository containing omeprazole complexes
AU Hwang, Sung-Joo; Park, Sung Bae; Rhee, Gye Ju
CS College Pharmacy, Chungnam National University, S. Korea
SO Yakche Hakhoechi (1995), 25(3), 227-37
CODEN: YAHAEX; ISSN: 0259-2347
PB Korean Society of Pharmaceutics
DT Journal
LA Korean
AB Omeprazole (OMP) complexes such as inclusion complexes with hydroxypropyl-β-cyclodextrin (HPCD) and β-cyclodextrin(β-CD), OMP-cholestyramine (CHL) and OMP-ethylenediamine (OMP-ED) were prepared, resp. The partition coeffs. in Witepsol H-15/pH 7.4 phosphate buffer solution of OMP complexes (OMP-HPCD: 3.69±0.26, OMP-β-CD: 4.08±0.21, OMP-CHL: 4.36±0.25 and omeprazole sodium (OMP-Na): 3.64±0.37) were higher than that of OMP (2.66±0.47). OMP was not completely dissolved until even 3 h, but all the OMP complexes studied were released about 100% in 20 min. The rectal suppositories containing OMP or each of OMP complexes were prepared using Witepsol H-15 base, and their dissoln. and stability were examined, and pharmacokinetic study were investigated after their rectal administrations to the rabbits. While drug release from OMP-containing suppository was less than 60% in 150 min, drug release from suppositories containing OMP-β-CD, OMP-CHL, OMP-Na and OMP-ED was about 65% in 20 min. Expecially, OMP-HPCD suppository released OMP about 70% in 10 min. All the additives such as sodium lauryl sulfate, eglumine, arginine and PVP increased drug release from OMP-HPCD suppository to some extent. The decomposition rate consts. of OMP in the suppositories were 9.117+10-3 day-1 for OMP suppository, 2.121+10-2 for OMP-HPCD, 1.607+10-2 for OMP-β-CD, 9.26+10-3 for OMP-Na, 6.769+10-3 for OMP-CHL and 5.58+10-3 day-1 for OMP-ED suppository, resp. Additives such as

arginine, eglumine and ED had some stabilizing effect for OMP-HPCD, OMP-CHL and OMP-Na suppositories, resp. After 6 mo-storage at 30°C, 75% RH, OMP-CHL suppository was most stable. The values of Tmax for OMP-HPCD and OMP-Na suppositories were 11.7±2.36 and 11.4±2.56 min, resp. The values of Cmax for OMP-HPCD and OMP-CHL suppository were 2.31 μg/mL ($p<0.01$) and 1.89 μ/mL ($p<0.01$), resp. The values of AUC for OMP and OMP-β-CD suppository were 61.9±25.79 and 68.6±29.48 μg·min/mL, and the corresponding values for OMP-HPCD and OMP-CHL were 106.1±43.16 ($p<0.05$) and 127.3±42.52 μg·min/mL($p<0.01$), resp. The above results indicate the OMP-HPCD and OMP-CHL suppositories have the excellent bioavailabilities in vivo study.

L1 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:636883 CAPLUS
DN 123:65726
TI Ethylenediamine complex for stabilization of omeprazole
AU Oh, Sea Jong; Kim, Eun Young; Kim, Kil Soo; Kim, Yuon Jeung; Rhee, Gye Ju
CS College Pharmacy, Chungnam National University, Taejon, 305-764, S. Korea
SO Yakche Hakhoechi (1995), 25(1), 9-17
CODEN: YAHAEX; ISSN: 0259-2347
PB Korean Society of Pharmaceutics
DT Journal
LA Korean
AB To stabilize omeprazole (OMP), ethylenediamine (ED) complex of omeprazole (OMPED) was prepared by reaction between OMP and ED in methanol, and the complex formation was confirmed by the instrumental anal., i.e., IR, DSC, EA, NMR, MS and XRD. The rates of decomposition of OMP and OMPED in aqueous solution and the shelf lives at standard temperature were measured by accelerated stability anal. The results are summarized as follows; The mole role of OMP and ED in OMPED complex is 1:1, the energy of formation within OMPED might be combined between polar imidazole group of OMP with induced a dipole amine group in the readily polarizable ED mol. At standard temperature the degradation rate constant of OMP in aqueous solution is 2.540 + 10-2 hr-1 and the shelf life is 4.15 h, and in the case of OMPED the degradation rate constant is 7.986 + 10-4 hr-1 and the shelf life is 131.96 h. So, the OMPED has about 31 times longer shelf life than OMP. The activation energy of OMP and OMPED are 5.23 and 18.55 kcal mole-1 resp. The stability of OMP is dependent chiefly on pH in the solns. and it decomps. readily in acidic medium by hydrogen ion catalyzed reaction but becomes stable beyond pH 9.0. In case of the ED-complex, OMPED is stable in neutral as well as in dilute acidic solns. even in pH 6, OMPED is very stable to light (UV), i.e., the rate constant and shelf life of IMP are k = 1.0188 + 10-2 day-1. T90% = 4.5 days, on the other hand, those of OMPED are k = 7.138 + 10-4 day-1, T90% = 64.1 days, resp. From the above results, it is thought that new dosage forms could be developed by using the OMPED as a potential OMP complex.

L1 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:638249 CAPLUS
DN 121:238249
TI Development of a new omeprazole-ion exchange resin complex
AU Rhee, Gye Ju; Lee, Ki Myung; Kim, Eun Young; Lee, Chang Hyun; Hwang, Sung-Joo
CS College of Pharmacy, Chungnam National University, Taejon, 305-764, S. Korea
SO Yakhak Hoechi (1994), 38(3), 250-64
CODEN: YAHOA3; ISSN: 0513-4234
DT Journal
LA Korean
AB Omeprazole(OMZ)-cholestyramine(CHL) and various OMZ-Dowex resin complexes

were prepared by reaction between OMZ and activated resins in 0.1N NaOH solution and their phys. properties were tested by means of IR, differential scanning calorimeter(DSC), x-ray diffraction. Chemical stability of OMZ-CHL was increased markedly compared with OMZ and the decomposition of OMZ-CHL followed the pseudofirst-order kinetics and the rate consts. were 2.743 + 10-4/day at 20°, 7.83 + 10-3/day under 80% RH and 1.68 + 10-2/day under UV radiation, resp. On the other hand, the rate consts. of OMZ were 2.996 + 10-4/day at 20°, 1.17 + 10-2/day under 85% RH, and 4.07 + 10-2/day under UV radiation, resp. The rates of dissoln. of OMZ-CHL bulk and OMZ-CHL tablet were 100% and >85% in 15 min, resp., which were higher than OMZ base and OMZ-tablet. In the acute toxicol. test, the value of oral LD50(mouse) was 4.608 g/kg. OMZ-CHL was pelletized using lactose, PEG, D-sorbitol, Avicel PH 101, sodium laurylsulfate and PVP K-30 and enteric coated with HPMCP, Myvacet, acetone, ethanol and cetanol, of which dissoln. rate was found to be more than 85% in 10 min. From the above results, it was found that OMZ-CHL is a useful means for development of new oral dosage forms of OMZ.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	22.38	22.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.38	-4.38

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